R E M A R K S

Claim Amendments

The end of each of claims 12 and 15 was amended to add a feature supported on page 7, lines 9 to 14 of the specification.

Claim 13 was amended to depend on claim 11.

Claim 16 was amended to depend on claim 14.

Allowable Subject Matter

Applicants are pleased to note that claims 11 and 14 were considered to be allowable and that claims 13 and 16 were objected to only as being dependent on a rejected claim (see the bottom of page 2 of the January 20, 2010 Office Action).

Applicants' Present Claims 12 and 15

Applicants' present claim 12 is directed to a clear ophthalmic solution. Applicants' present claim 15 is directed to a method of preventing white turbidity in an ophthalmic solution. The ophthalmic solution recited in applicants' present claims 12 and 15 comprises (i) latanoprost, (ii) benzalkonium chloride and (iii) at least one agent selected from the group consisting of glycerin, polyethylene glycol, propylene glycol and trehalose,

wherein the solution is characterized as being a clear ophthalmic solution without white turbidity due to a change of formulation.

Obviousness Rejection Under 35 USC 103

Claims 12 and 15 were rejected under 35 USC 103 as being unpatentable over Dean et al. (USP 6,166,073) in view of Patent Abstract of Japan (JP 62-277323) to Kurasawa et al. and further in view of Hellberg et al. (USP 6,646,001) for the reasons indicated on page 2 of the January 20, 2010 Office Action.

It was admitted in the previous Office Action of September 9, 2009 that Dean et al. do not teach agents such as glycerin, polyethylene glycol, propylene glycol, mannitol or trehalose.

Dean et al. (USP 6,166,073) relate to a composition for treating ocular hypertension comprising a combination of a DP-agonist prostaglandin and a FP-agonist prostaglandin.

Dean et al. do not teach or suggest that glycerin, polyethylene glycol, propylene glycol and/or trehalose can be added to their composition. Moreover, Dean et al. do not teach or suggest the problem of white turbidity due to a change of formulation, let alone a means to avoid such problem.

Kurasawa et al. (JP 62-177323) relate to a method of formulating an eyedrop comprising ketotifen fumarate. Kurasawa et al. do not teach or suggest the use of latanoprost . Kurasawa et al. do not address the problem of a change of formulation by latanoprost and benzalkonium chloride, let alone a means to avoid such problem.

Hellberg et al. (USP 6,646,001) relate to a composition for treating ocular hypertension comprising a prostaglandin FP receptor agonist and a prostaglandin synthesis inhibitor. However, Hellberg et al. do not teach or suggest the addition of glycerin, polyethylene glycol, propylene glycol and/or trehalose. Hellberg et al. do not address the problem of white turbidity due to a change of formulation, let alone a means to avoid such problem.

As discussed above, none of the references teach or suggest the problem of white turbidity due to a change of formulation in an eyedrop comprising latanoprost and benzalkonium chloride, let alone a means to avoid such problem. Dean et al. and Hellberg et al. do not teach or suggest the use of glycerin, polyethylene glycol, propylene glycol and/or trehalose. Kurasawa et al. disclose that a polyhydric alcohol such as glycerin, polyethylene

glycol, propylene glycol and trehalose can be added as a tonicity agent, but use ketotifen fumarate which has a completely different chemical structure from latanoprost, a prostaglandin.

It is therefore respectfully submitted that one of ordinary skill in the art would not consider to combine the references in the manner set forth in the January 20, 2010 Office Action. Even assuming *arguendo* that the references were combinable, for the reasons discussed hereinabove, it is respectfully submitted that a person of ordinary skill in the art would not arrive at applicants' present claims 12 and 15 from the combined disclosures of the references.

Based on the comparative formulations 3 and 4 in Table 1 on page 18 of the present specification, it was confirmed that an eyedrop comprising latanoprost and benzalkonium chloride turns cloudy white due to a change of formulation (see Table 5 on page 24 of the present specification). In contrast thereto, according to applicants' present claims 12 and 15, the addition of glycerin, polyethylene glycol, propylene glycol and/or trehalose prevents white turbidity and a clear ophthalmic solution is provided (see Table 4 on page 21 of the present specification and Table 6 on page 26 of the present specification).

The results discussed in the preceding paragraph were confirmed in the DECLARATION UNDER 37 CFR 1.132 of Hiroyuki ASADA dated January 20, 2009 ("January 20, 2009 ASADA DECLARATION"). In the January 20, 2009 ASADA DECLARATION, additional experiments were carried out following the same procedure as in Experiment 1-1) of the present specification for the case where the concentration of BAK is 0.007% or 0.003%. The following Table (a) shows results that were set forth in the January 20, 2009 ASADA DECLARATION.

Table (a)

	Comparative formulation A-1	Comparative formulation A-2
Latanoprost	0.005	0.005
Crystalline sodium dihydrogenphosphate	0.2	0.2
Sodium chloride	0.9	0.9
BAK	0.007	0.003
Diluted hydrochloric acid	q.s.	q.s.
Sodium hydroxide	q.s.	q.s.
Purified water	q.s.	q.s.
Appearance	White turbidity	Slightly white turbidity

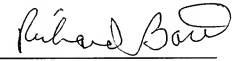
(Unit in Table: % (W/V), q.s.: quantum sufficient)

Withdrawal of the 35 USC 103 rejection is accordingly respectfully requested.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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